GLUTATHIONE AS IT RELATES TO HIV/AIDS

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HIV disease is now considered to be the most serious health problem in the world today, especially in the developing countries. It is particularly destructive to T lymphocytes, especially CD4+ T cells, and a state of profound immune deficiency is seen in the affected individual. This, in turn, leads to a whole host of complications, resulting in an acquired immune deficiency syndrome, AIDS. Typically, the patient becomes susceptible to certain types of pneumonia, diarrhea, candida and unusual cancers. Finally there is malnutrition, wasting and death. All of this may take years to develop, however, especially with the current antiretroviral therapies now available in the Western world.

It has been well established that the glutathione pool is unusually low in individuals with HIV/AIDS (1,2). This can be attributed partly to chronic oxidative stress (3). Cysteine deficiency provides another compelling explanation for the observed deficiency since this amino acid is the rate-limiting precursor amino acid for glutathione synthesis. Thus, Droge et al. have estimated that HIV+ patients experience a massive loss of sulfur equivalent to 10g cysteine/day even when asymptomatic (4).

Glutathione deficiency in HIV/AIDS is an important issue, contributing to many of the complications of this disease, particularly the immune deficiency. Thus, many lymphocyte functions are compromised by low glutathione such as antigen processing, proliferation during clonal expansion, destruction of virally infected cells or cancer cells by cytotoxic T cells or NK cells (3,5). Furthermore, in glutathione depletion, there is a tendency for the humoral (antibody) response to predominate while the cell-mediated response is reciprocally inhibited (5). Cell mediated immunity provides the effective defense mechanism in many viral infections and cancer, and this is true in HIV/AIDS. Indeed a correlation has been observed in HIV+ individuals between progression of disease and a shift from cell mediated to humoral response (as measured by cytokine production by T helper cells) (6). Furthermore, the prooxidant/antioxidant (redox) status in the cell is controlled to a large extent by glutathione. An imbalance of redox status indirectly results in up-regulation of (a) inflammatory cytokines such as TNF alpha, which promotes wasting, (b) increased viral replication and (c) increased apoptosis, increasing the death of CD4+ T cells (3,6). (Refer to 'The Immune System: Role of Glutathione for further details).

Glutathione deficiency also has a major effect on other systems and organs in the body. The lungs, for example, utilize and consume glutathione to counter oxidative stress associated with tissue oxygenation and antimicrobial phagocyte function, as well as for detoxification of inhaled toxins. Thus, pulmonary disease is frequently associated with AIDS. Similar arguments can be applied to the intestinal disorders and neurological problems seen in AIDS patients.

In 1997 Herzenberg et al. showed that there was a direct correlation between low T lymphocyte glutathione values and impaired survival of the individual (1). Obviously it is of paramount importance to replenish glutathione levels in HIV+ individuals by providing the precursor amino acid cysteine. N-acetyl cystine can be effective in this regard and can increase the probability of survival (1,7,8). However, the side effects of this drug are considerable (9), especially in debilitated AIDS patients. Immunocal®, on the other hand, is proven to raise intracellular glutathione (9), by delivering cysteine in a bioavailable form to the cells to be made into glutathione. It has no known toxicity, does not interfere with any other drug regimen being given and has been used successfully in HIV+ individuals (10,11).

References

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